

II. RESPONSE

A. Status of the Claims

Claims 67 and 86-89 were pending prior to the Office Action dated March 17, 2005. These claims were rejected in that Office Action. In a subsequent communication from Examiner Crouch (mailed August 5, 2005), which Applicant's representative appreciates, the rejection of claims under 35 U.S.C. 103 was withdrawn. Therefore, the claims remain rejected under the judicially created doctrine of obviousness-type double patenting and written description.

B. Obviousness-Type Double Patenting Rejection Is Inconsistent with Procedure with Prior Patent

Applicant is submitting the following arguments to complete the record for possible appeal. These arguments were previously submitted to the Examiner in preparation for a telephone conference that was kindly granted by Examiner and Supervisory Examiner Deborah Reynolds.

The present application contains five claims (claims 67 and 86-89), all of which are directed to "pharmaceutical compositions." The above-referenced application ("the '681 application") has several outstanding rejections including an obviousness-type double patenting rejection. In the Office Action Dated March 17, 2005, all of the claims were rejected under the judicially created doctrine of obviousness-type double patenting over various **composition** claims not reciting a "**pharmaceutical** composition" in different patents.¹ This rejection is inconsistent with the PTO's previous position in a related and issued case with respect to the

¹ Claims were also rejected under the doctrine of obviousness-type double patenting over *pharmaceutical* composition claims in issued patents. This basis for the rejection is not relevant to the issue presently being raised. Moreover, if the pharmaceutical composition claims in the present case were deemed allowable, Applicant would submit a terminal disclaimer, if appropriate, over the patents with pharmaceutical composition claims.

separate patentability of **pharmaceutical** composition claims and it may create an issue of validity regarding certain claims in issued patents.

The relevant basis for the rejection is as follows:

- 1) claims 22 and 37 of Application No. 08/626,678 (now Patent No. 6,905,873) (“the ’678 application”), which are said to be drawn to recombinant adenovirus, which carries an adenovirus vector construct comprising an expression region encoding p53 under the control of a CMV IE promoter and an adenovirus vector construct comprising an expression region encoding p53 under the control of a CMV IE promoter;
- 2) claims 1-3, 5, 8-10, 12, and 15-18 of U.S. Patent No. 6,410,010, which are said to be drawn to recombinant adenovirus with constructs comprising an expression region encoding p53 under the control of a CMV IE promoter;
- 3) claims 1, 7, and 12 of U.S. Patent No. 6,511,847, which are said to be drawn to an adenovirus expression vector comprising an ITR and a p53 gene under the control of a CMV promoter.

Generally, the Action rejects **pharmaceutical** composition claims under obviousness-type double patenting over adenovirus or adenovirus expression vector claims (“**composition** claims”) in issued patents.

1. The Inconsistency with the Position Previously Taken by PTO in Issued Patents

While in the present case **pharmaceutical** composition claims have been rejected over **composition** claims under obviousness-type double patenting, another examiner took a contrary position during the prosecution of two previous applications that claim priority to the same priority patent application of the present case.

During the prosecution of USN 08/459,713 (now U.S. Patent No. 6,740,320) (“the ’713 application”), Examiner David Guzo rejected method claims over pharmaceutical claims in co-pending application USN 08/626,678 (now U.S. Patent No. 6,905,873) (“the ’678 application”). Similarly, he rejected the pharmaceutical composition claims in the ’678 application over the method claims in the ’713 application. As a result of those positions taken by Examiner Guzo,

Applicants cancelled the pharmaceutical composition claims in the '678 application and added them to the '713 application. This is discussed in further detail below and a timeline is provided to depict this (Exhibit 1).

a) Prosecution of the '713 case

During the prosecution of the '713 application, method claims in the '713 application (generally directed to methods of treating cancer with adenovirus comprising wild-type p53) were rejected under a provisional non-obviousness-type double-patenting rejection (Office Action dated January 4, 2001). The rejection of the method claims was based on claims 29-32 and 34-35 of the co-pending and related '678 application. Claims 29-32 and 34-35 of the '678 application were pharmaceutical composition claims. The January 4, 2001 Action in the '713 patent application stated that “[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the claims in the '678 application recite pharmaceutical compositions comprising recombinant adenoviral vectors capable of expressing the p53 gene, wherein said pharmaceutical compositions are designed to be administered to humans for treatment of cancer (as per the instant claims).” Page 7. In other words, the examiner in the '713 case went on record as saying that Ad-p53 pharmaceutical composition claims and methods of treatment claims using Ad-p53 were not “patentably distinct.” Applicant notes that this is not a statement regarding search burdens but an affirmative statement regarding what is “PATENTABLE (novel and nonobvious) over each other.” *See* MPEP § 803 (defining what “distinct” means).

Applicants responded to the January 4, 2001 Office Action saying that the rejections were provisional and that the substance of the rejections would not be addressed at that time.

b) Prosecution of the '678 case

Similarly, in the prosecution of the '678 application, the method claims of the present case were cited in a provisional obviousness-type double-patenting rejection of the pharmaceutical composition claims. (Office Action dated July 11, 2001). That Office Action stated: "It would have been obvious for the ordinary skilled artisan to use the instantly claimed pharmaceutical compositions in the methods of treated cancers recited in the '713 application because said pharmaceutical compositions are designed to treat cancer by introducing normal p53 coding regions to cancer cells which lack a normal p53 gene." Pages 5-6.

In response to the July 11, 2001 Office Action in the '678 case, Applicants traversed the provisional obviousness-type double-patenting rejection (Response to Office Action dated July 11, 2001). They argued the double-patenting rejection was inappropriate because a restriction requirement had been sent out by the Patent Office in the parent application (08/145,826) in which the adenoviral composition claims were restricted from the treatment method claims (Restriction Requirement). In the subsequent Office Action, however, the Action indicated this argument was not persuasive (Office Action dated January 3, 2002). It stated that the basis for the rejection was not the adenoviral composition claims, but specifically the pharmaceutical composition claims. It further said: "Clearly, the instantly claimed pharmaceutical compositions comprising recombinant adenoviruses capable of expressing wild-type p53 are obvious over claims (pending in the '713 application) reading on a method of treating cancers in patients comprising administering pharmaceutical compositions comprising recombinant adenoviruses capable of expressing wild-type p53 because the method claims (in the '713 application) merely recite the intended use of the instantly claimed pharmaceutical compositions." Page 7.

While the claims in the '678 application were eventually allowed, the reason for the allowance was that the double-patenting rejections were all provisional. Applicants subsequently

canceled the pharmaceutical composition claims in the '678 application and filed a continuation application because of the Patent Office's position.

Meanwhile, Applicants filed claims 75-101, which are directed to pharmaceutical compositions, in the '713 application. Applicants reasoned that this was appropriate as a result of the Patent Office's double-patenting position in this case and the '678 application. Some of the added claims are nearly identical in scope to the claims canceled in the '678 application. Furthermore, even if some of the claims were of a different scope, nothing in the Office Actions concerning the double-patent rejections would indicate that the scope can be the basis for distinguishing the pharmaceutical composition claims from the method of treatment claims as a separately patentable invention. As indicated in the Office Actions of these other cases, the Patent Office's opinion was that pharmaceutical compositions comprising recombinant adenoviruses capable of expressing wild-type p53 are not patentably distinct with respect to methods of treating cancers in patients comprising administering recombinant adenoviruses capable of expressing wild-type p53. Consequently, Examiner Guzo permitted claims 75-101 to be added into the '713 application and he subsequently allowed the case.

2. Relevance to Current Application

The Office Action Dated September 3, 2003 generally takes the position that a "pharmaceutical composition" claim is similar to a composition claim and that "[i]t is the products, the pharmaceutical compositions comprising adenovirus, that is claimed; not the methods of gene therapy." Action at page 12. This position is repeated in subsequent office actions. In fact, the pharmaceutical composition claims in this application are rejected over the **composition** claims in the same '678 application discussed above (which issued without pharmaceutical composition claims).

This position is in marked contrast to the previous position upheld by the PTO, that pharmaceutical composition claims were distinct from non-pharmaceutical composition claims because only the former were obvious over methods claims, while the latter were patentably distinct from method claims. It is inconsistent and, thus, improper for the PTO to now to take this new position. Moreover, Applicant points out the fundamental unfairness of switching positions at this point, particularly given Applicant's reliance on the PTO's stance in earlier prosecutions. These issues could significantly affect patent term and the validity of **issued patents** and allowed patent applications.

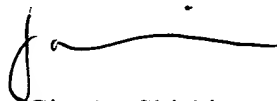
C. Written Description

The arguments regarding written description have been previously provided. Applicant does not have further submissions at this point. Applicant urges the reconsideration of the obviousness-type double patenting issue because of its potential ramifications with issued U.S. Patents.

CONCLUSION

Applicant solicits any recommendations regarding how to address the current issue in the context of those issued patents.

Respectfully submitted,



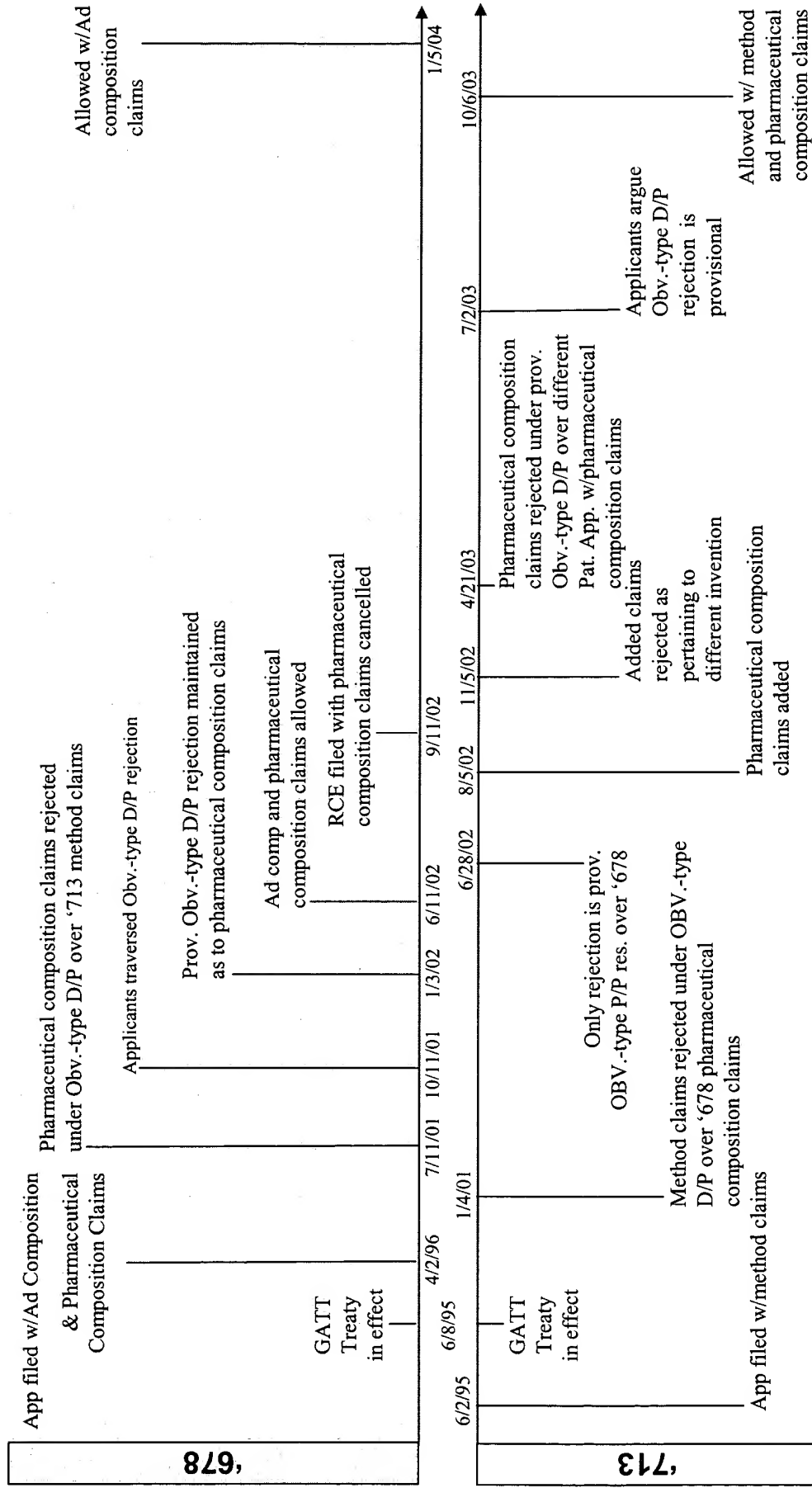
Gina N. Shishima
Reg. No. 45,104
Attorney for Applicant

FULBRIGHT & JAWORSKI L.L.P.
600 Congress Avenue, Suite 2400
Austin, Texas 78701
(512) 474-5201
(512) 536-4598 (facsimile)

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Exhibit 1

Timeline for relevant issues during prosecution of '678 and '713 applications



'678 application relevant claim

29. A pharmaceutical composition comprising:

- a recombinant adenovirus which carries an adenovirus vector construct comprising an expression region encoding p53 under the control of a cytomegalovirus IE promoter; and
- a pharmaceutically acceptable carrier, excipient, or diluent.

'713 application relevant claim

9. A method of treating a human cancer patient having a human malignancy comprising administering to said patient an amount of an adenovirus composition effective to inhibit said malignancy, wherein said adenovirus composition comprises an adenovirus vector construct comprising a wild-type p53 gene under the control of a promoter, dispersed in a pharmacologically acceptable solution.